Network Systems
Science & Advanced
Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

January 27th, 2021

(data current to January 25th-26th)
Biocomplexity Institute Technical report: TR 2021-011



BIOCOMPLEXITY INSTITUTE

biocomplexity.virginia.edu

About Us

- Biocomplexity Institute at the University of Virginia
 - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
 - Pandemic response for Influenza, Ebola, Zika, and others



Points of Contact

Bryan Lewis brylew@virginia.edu

Srini Venkatramanan srini@virginia.edu

Madhav Marathe marathe@virginia.edu

Chris Barrett ChrisBarrett@virginia.edu

Biocomplexity COVID-19 Response Team

Aniruddha Adiga, Abhijin Adiga, Hannah Baek, Chris Barrett, Golda Barrow, Richard Beckman, Parantapa Bhattacharya, Andrei Bura, Jiangzhuo Chen, Clark Cucinell, Patrick Corbett, Allan Dickerman, Stephen Eubank, Arindam Fadikar, Joshua Goldstein, Stefan Hoops, Ben Hurt, Sallie Keller, Ron Kenyon, Brian Klahn, Gizem Korkmaz, Vicki Lancaster, Bryan Lewis, Dustin Machi, Chunhong Mao, Achla Marathe, Madhav Marathe, Fanchao Meng, Henning Mortveit, Mark Orr, Joseph Outten, Akhil Peddireddy, Przemyslaw Porebski, SS Ravi, Erin Raymond, Jose Bayoan Santiago Calderon, James Schlitt, Aaron Schroeder, Stephanie Shipp, Samarth Swarup, Alex Telionis, Srinivasan Venkatramanan, Anil Vullikanti, James Walke, Andrew Warren, Amanda Wilson, Dawen Xie



Overview

• Goal: Understand impact of COVID-19 mitigations in Virginia

Approach:

- Calibrate explanatory mechanistic model to observed cases
- Project based on scenarios for next 4 months
- Consider a range of possible mitigation effects in "what-if" scenarios

Outcomes:

- Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
- Geographic spread over time, case counts, healthcare burdens

Key Takeaways

Projecting future cases precisely is impossible and unnecessary. Even without perfect projections, we can confidently draw conclusions:

- Case rate growth in Virginia has slowed but remains high
- VA mean weekly incidence down sharply 54/100K from 72/100K, as national levels continued to decline (to 45/100K from 54/100K)
- Projections are mixed across commonwealth with some short-term growth at state level mainly driven by central section of the state
- Recent updates:
 - Adjusted projection window to account for shifting trends
 - Scenarios based on past control levels (best and fatigued) and emerging new variants with enhanced transmissibility
 - Further updates to vaccination schedules, accounts for partial protection from first dose and merges observed doses with goals for future vaccine administration
- The situation is changing rapidly. Models will be updated regularly.



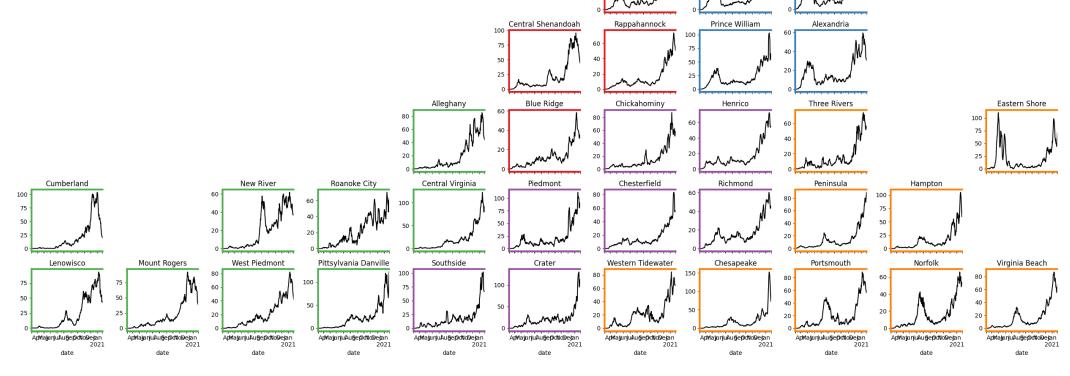
Situation Assessment



Case Rate (per 100k) by VDH District

Surging Rates subside and start declining

- Majority of districts have decreasing rates
- Rates remain high in many districts





Test Positivity by VDH District

Weekly changes in test positivity by district

 Increasing levels in many districts throughout the commonwealth with many districts above 10% for several weeks

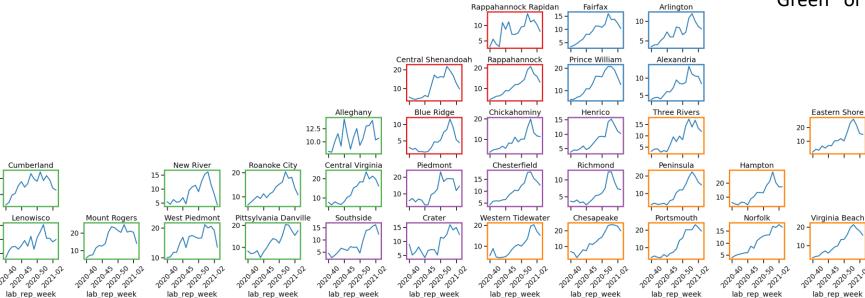
 Slight reduction of 115 counties, down from 125, over 10% (as of Jan 20th)

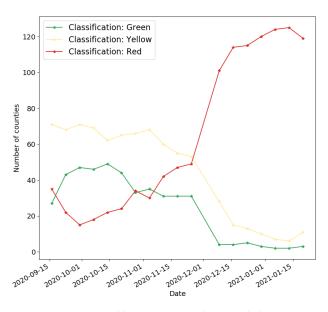


Green: Test positivity <5.0% (or with <20 tests in past 14 days)

Yellow: Test positivity 5.0%-10.0% (or with <500 tests and <2000 tests/100k and >10% positivity over 14 days)

Red: >10.0% and not meeting the criteria for "Green" or "Yellow"





■ University of Virginia

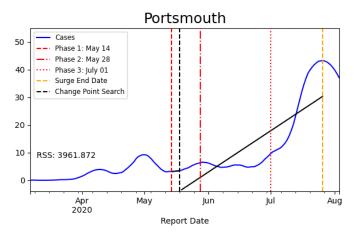
https://data.cms.gov/stories/s/q5r5-gjyu

District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

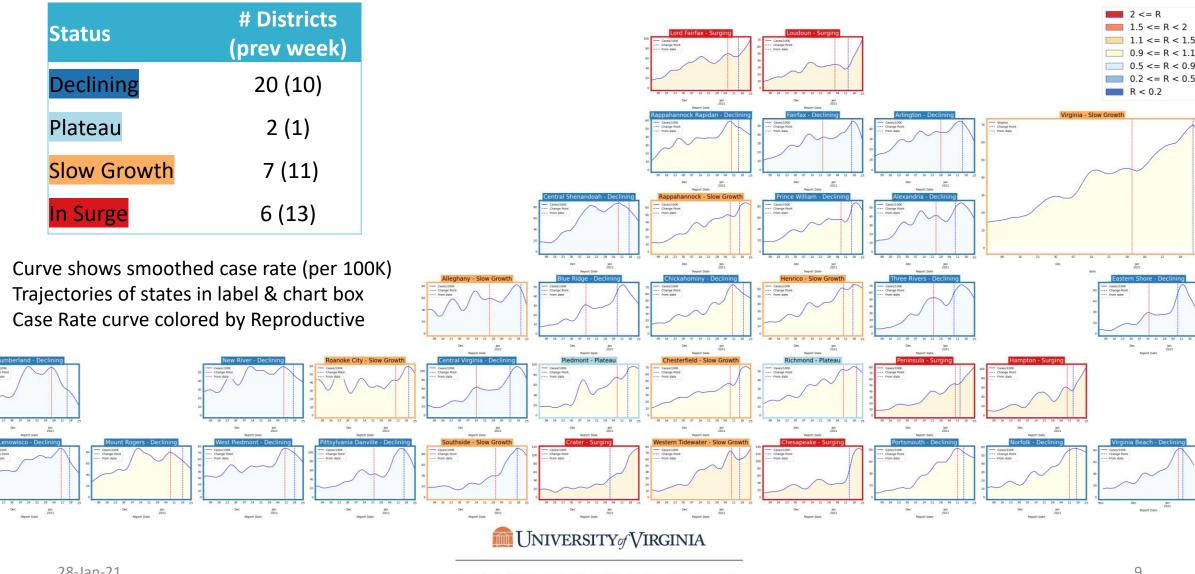
Hockey stick fit



Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	20 (10)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	2 (1)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	7 (11)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	6 (13)



District Trajectories – last 10 weeks



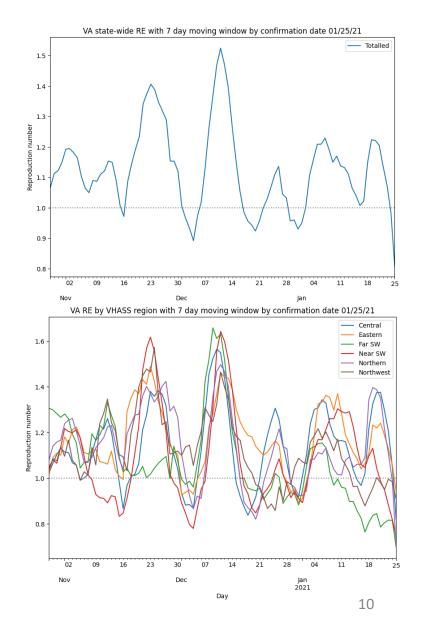
Estimating Daily Reproductive Number

Jan 25th Estimates

Region	Date Confirmed R _e	Date Confirmed Diff Last Week
State-wide	0.809	-0.340
Central	0.820	-0.398
Eastern	0.942	-0.167
Far SW	0.698	-0.109
Near SW	0.746	-0.351
Northern	0.708	-0.636
Northwest	0.910	-0.010

Methodology

- Wallinga-Teunis method (EpiEstim¹) for cases by confirmation date
- Serial interval: 6 days (2 day std dev)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill



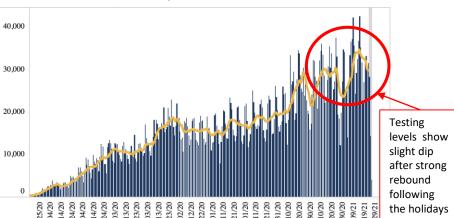
^{1.} Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Changes in Case Detection

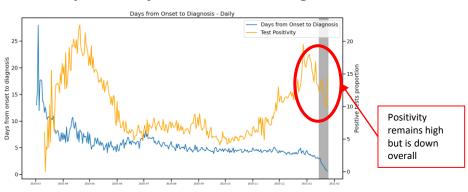
7-Day Moving Average

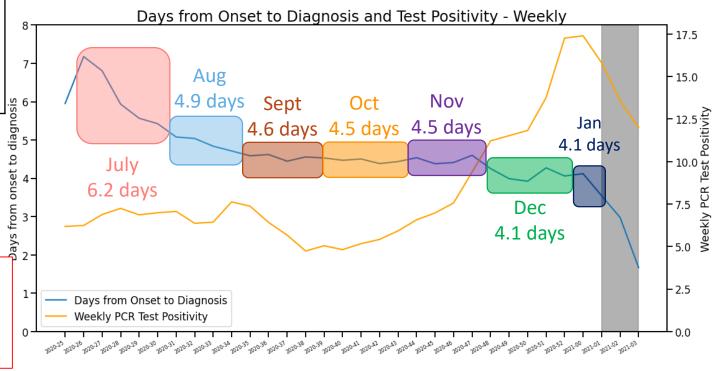
Timeframe (weeks)	Mean days	% difference from overall mean
May (17-21)	5.7	-21%
June (22-25)	5.8	-19%
July (26-30)	6.2	-14%
Aug (31-34)	4.9	-32%
Sept (35-38)	4.6	-37%
Oct (39-43)	4.5	-38%
Nov (44-47)	4.5	-38%
Dec (48-49)	4.1	-43%
Jan (00-01)	4.1	-47%
Overall (13-01)	7.2	
Number of Testing Engagetons by Lo	Number of Testing Encounters	

Number of Testing Encounters by Lab Report Date - All Health Districts, PCR Only

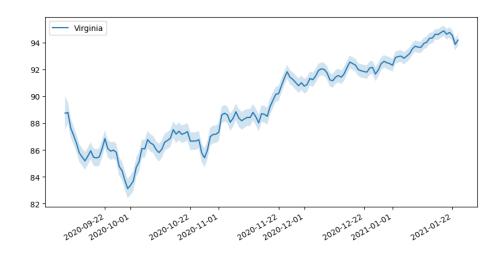


Test positivity vs. Onset to Diagnosis





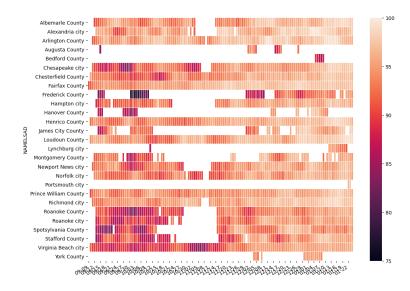
Mask usage in Virginia



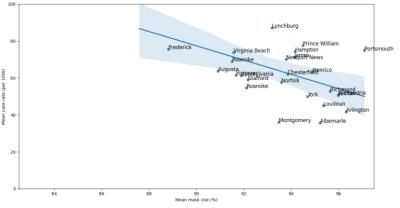
State level mask usage as reported via Facebook surveys has shown steady increase over past three months

- ~88% (early Nov) to ~94% (mid Jan)
- Some variance across the commonwealth
- ~3000 daily responses from VA

Data Source: https://covidcast.cmu.edu



Some county level fluctuations since beginning of Sept., though data quality may be affected by sample sizes



Correlations seen among VA counties between mask use and case rate are now stronger due to surging growth

Slope: - 3.8; for every % we see a ~4/100K case rate difference

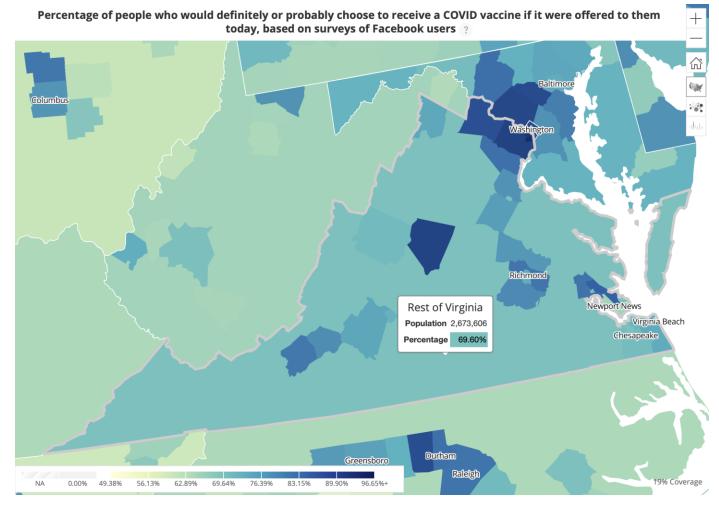


Vaccine Acceptance

Facebook administered survey:

Percent of people who would definitely or probably choose to receive a COVID vaccine if offered today

VA typically achieves 50-60% coverage with seasonal influenza vaccine (typically over the course of 3 months)



COVIDcast Data Explorer
Source: https://covidcast.cmu.edu



Health Care Worker Prevalence (per 100K)

Case Rates among health workers compared to population in last week

 Based on census counts of patient-facing health care workers (Practitioners and Technologists)

Prevalence rates for week ending Jan 9th

Buchanan

Russell

Washington

Tazewell

Smyth

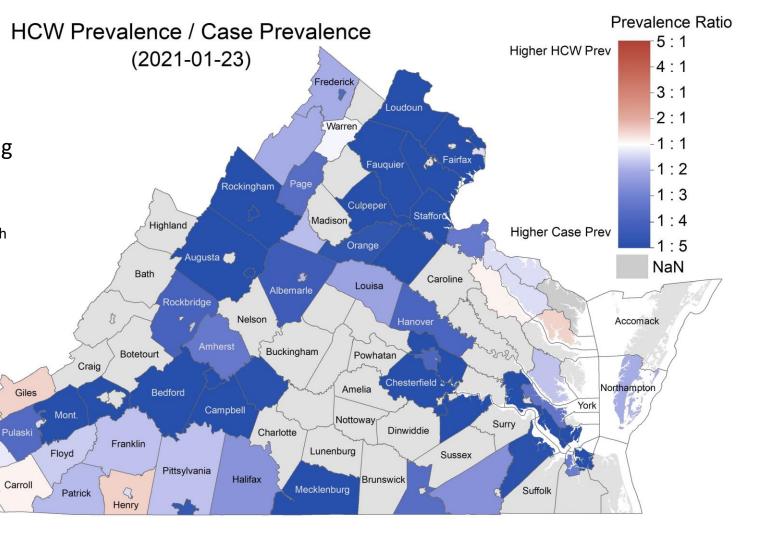
Bland

Wythe

Grayson

 HCW burden remains high in some Eastern counties as well as Southwest

Scott





Race and Ethnicity – Recent Rate Changes (per 100K)

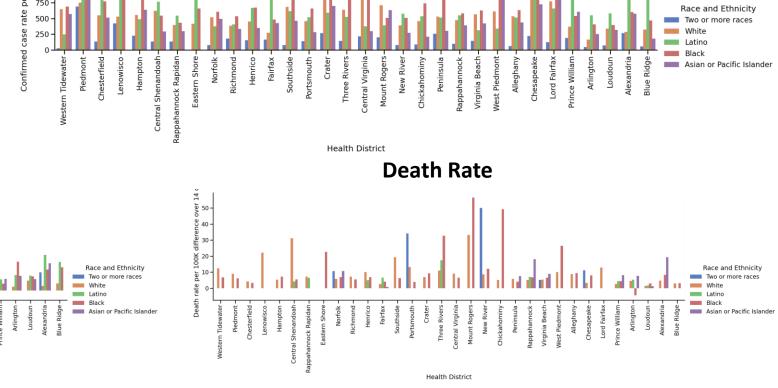
1750

¥ 1250 ·

Recent Changes in Race and Ethnicity Rates (per 100k)

- Two week change in population level rates
- Black, Latinx and 2 or more races populations have much higher changes in rates; disparity is more pronounced in some districts than others
- Based on 2019 census race-ethnicity data by county

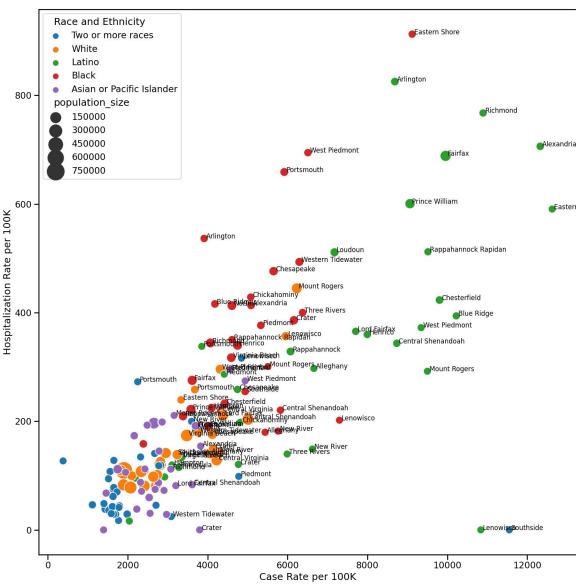
Hospitalization Rate



Case Rate



Race and Ethnicity cases per 100K



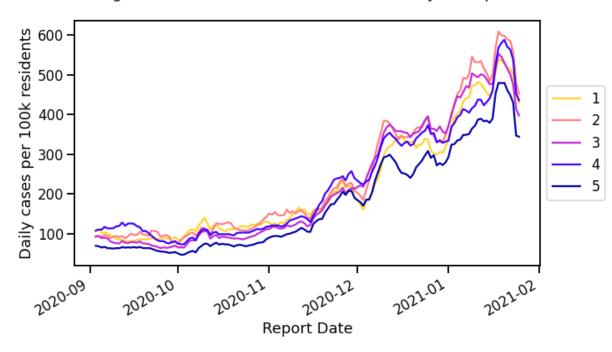
Rates per 100K of each Racial-Ethnic population by Health District

- Each Health District's Racial-Ethnic population is plotted by their Hospitalization and Case Rate
- Points are sized based on their overall population size
- Overlapping labels removed for clarity

28-Jan-21

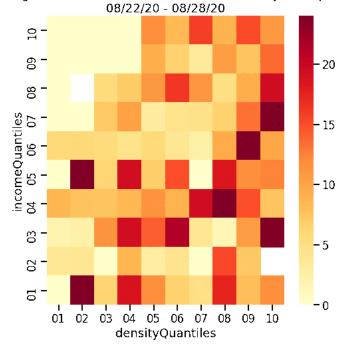
Impact across Density and Income

VDH 7-day moving average rate of new COVID-19 cases by zip code average household income (dollars/ household years) quantile



All zip codes show back into growth, wealthiest zip code now lags the rest significantly

VDH mean cases per 100k by zip code population density (person/ sq mile) and average household income (dollars/ household years) quantiles



Full evolution of pandemic, shows shifts from denser and wealthier zip codes to poorer and less dense zip codes



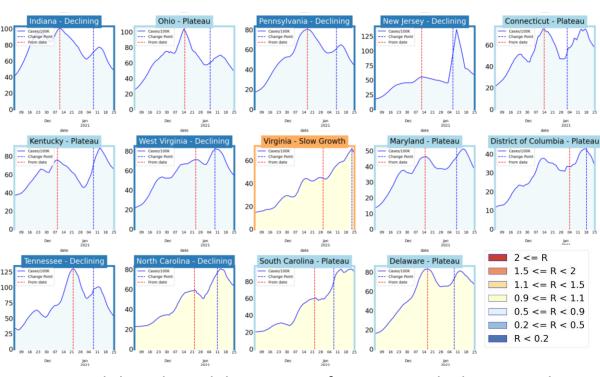
Other State Comparisons

Trajectories of States



 After a short rebound most states are plateauing (29) or declining (21)

Virginia and her neighbors



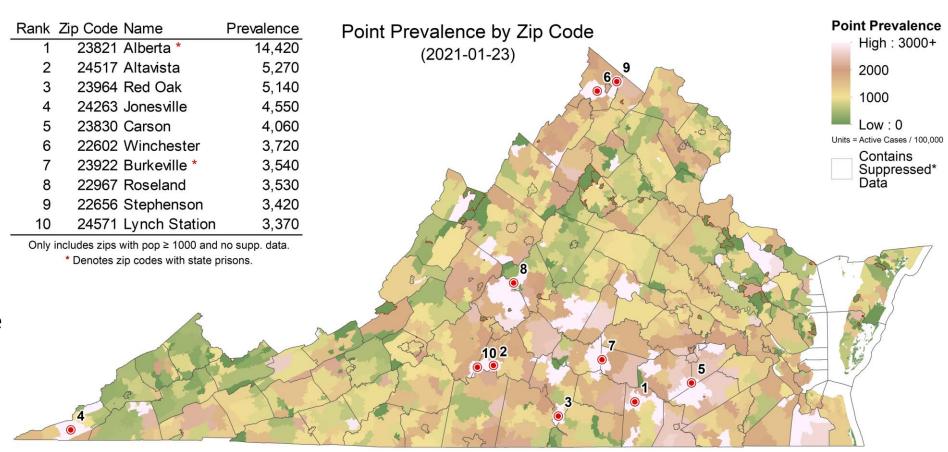
- VA growth has slowed, but is one of 3 states with slow growth
- VA and her neighbors remain relatively active compared to the rest of the US



Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

- Fewer prisons are in the top ten, most prisons seem to have intense rates for 2 to 3 weeks
- Concentrations of high rates in central and northwest regions
- Some counts are low and suppressed to protect anonymity, those are shown in white

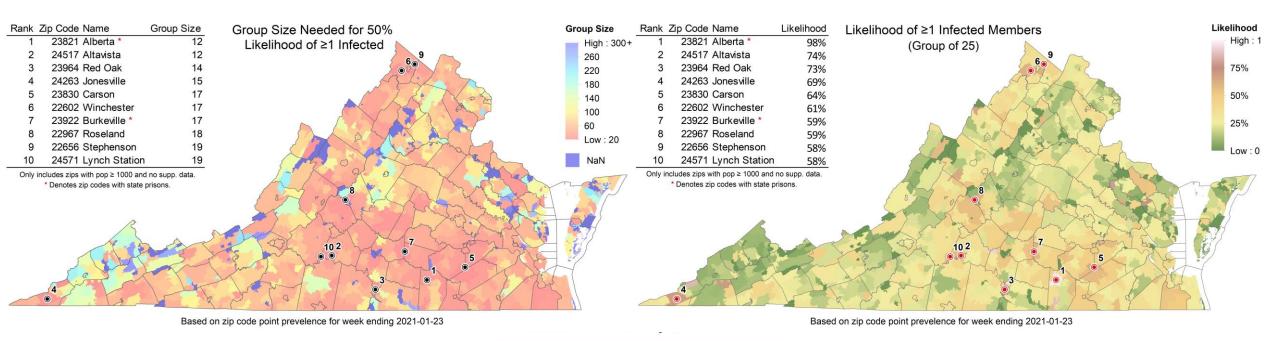




Risk of Exposure by Group Size

Case Prevalence in the last week by zip code used to calculate risk of encountering someone infected in a gathering of randomly selected people (group size 25)

- Assumes 3 undetected infections per confirmed case (ascertainment rate from recent seroprevalence survey)
- On left, minimum size of a group with a 50% chance an individual is infected by zip code (eg in a group of 20 in Staunton, there is a 50% chance someone will be infected)
- Some zip codes have high likelihood of exposure even in groups of 25



New variants of SARS-CoV2

Emerging new variants with increased transmissibility limited evidence of higher severity

• Evolution expected when virus under selective pressure

Lineage B.1.1.7

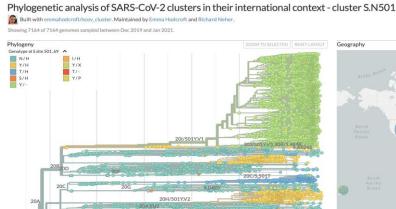
- B.1.1.7 has been detected in Virginia as well as in at least 293 cases across 25 states as of Jan 25th
- Given observed growth rate in UK and Denmark, estimate it will predominate in the US by mid-March
- <u>Recent study</u> suggests this variant may have higher mortality

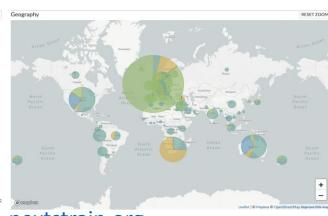
Lineage B.1.351

- Emerging strain in South Africa is also of concern for vaccine escape
- <u>Experiments</u> have demonstrated reduced potency of convalescent sera and monoclonal antibodies
- Moderna vaccine <u>demonstrated to have robust response</u> to this variant and thus likely to remain highly effective

Lineage P.1 (similar mutations as in B.1.1.7 and B.1.351)

- First case reported in Minnesota on Monday Jan 25th
- Emerging strain in the Amazon also shows potential of escaping existing immunity
- Resurgence of hospitalizations in Manaus, Brazil continues this despite estimated ¾ of the population infected





nextstrain.org

Model Update – Adaptive Fitting



Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection

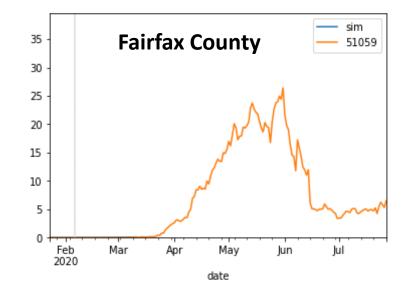
 Allows history to be precisely captured, and used to guide bounds on projections

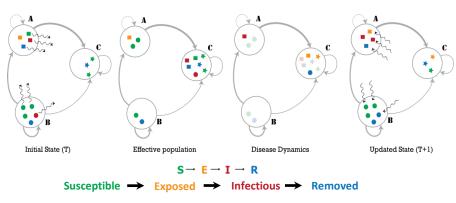
Model: An alternative use of the same meta-population model, PatchSim

- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Eliminates connectivity between patches, to allow calibration to capture the increasingly unsynchronized epidemic

External Seeding: Steady low-level importation

- Widespread pandemic eliminates sensitivity to initial conditions
- Uses steady 1 case per 10M population per day external seeding



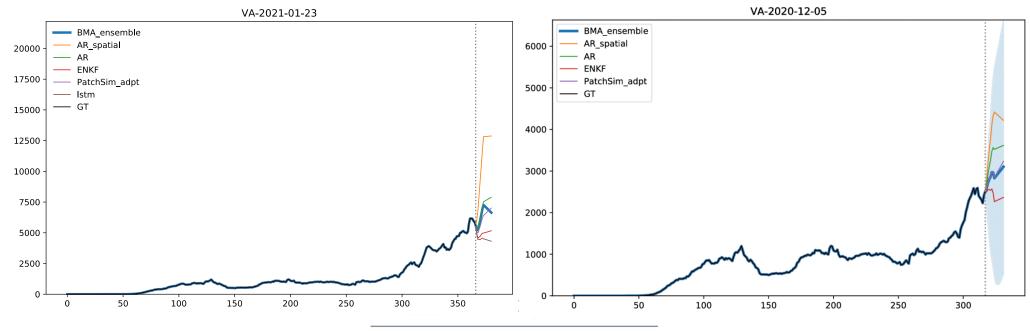




Using Ensemble Model to Guide Projections

An ensemble methodology that combines the Adaptive Fitting and machine learning and statistical models has been developed and refined

- Models: Adaptive Fitting, ARIMA, LSTM, AR, spatially driven AR, Kalman Filters (ENKF)
- This approach facilitates the use of other data streams (weather, mobility, etc.)
- Ensemble provides scaffolding for the Adaptive Fitting's short-term projections



28-Jan-21

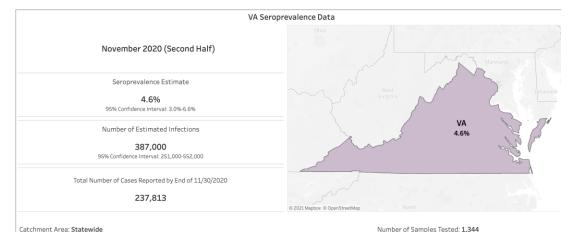
Seroprevalence updates to model design

Several seroprevalence studies provide better picture of how many actual infections have occurred

- Virginia Serology Study estimated 2.4% of Virginians estimated infected (as of Aug 15th)
- CDC Nationwide Commercial Laboratory Seroprevalence Survey estimated 4.6% [3.0% – 6.6%] seroprevalence as of Nov 12th – 26th up from 4.1% a month earlier

These findings are equivalent to an ascertainment ratio of ~3x, with bounds of (1x to 7x)

- Thus for 3x there are 3 total infections in the population for every confirmed case
- Uncertainty design has been shifted to these bounds (previously higher ascertainments as was consistent earlier in the pandemic were being used)



https://covid.cdc.gov/covid-data-tracker/#national-lab

Virginia Coronavirus Serology Project Interim findings by region and statewide - July 22, 2020

			Crude	Weighted preva	lence*
Region	Number of participants	Number antibody positive	prevalence per 100 participants	per 100 population	(95% CI)
Central	400	8	2.0	3.0	(0.5, 5.5)
East	707	9	1.3	1.5	(-0.2, 3.2)
Northern	819	36	4.4	4.2	(2.5, 5.9)
Northwest	756	11	1.5	0.9	(0.2, 1.6)
Southwest	431	3	0.7	1.0	(-0.2, 2.1)
Virginia	3,113	67	2.2	2.4	(1.6, 3.1)

^{*} Weighted prevalence is reweighted by region, age, sex, race, ethnicity, and insurance status to match census population.

https://www.vdh.virginia.gov/content/uploads/sites/8/2020/08/VDH-Serology-Projects-Update-8-13-2020.pdf



Calibration Approach

- Data:
 - County level case counts by date of onset (from VDH)
 - Confirmed cases for model fitting
- Calibration: fit model to observed data and ensemble's forecast
 - Tune transmissibility across ranges of:
 - Duration of incubation (5-9 days), infectiousness (3-7 days)
 - Undocumented case rate (1x to 7x) guided by seroprevalence studies
 - Detection delay: exposure to confirmation (4-12 days)
 - Approach captures uncertainty, but allows model to precisely track the full trajectory of the outbreak
- **Project:** future cases and outcomes generated using the collection of fit models run into the future
 - Mean trend from last 7 days of observed cases and first week of ensemble's forecast used
 - Outliers removed based on variances in the previous 3 weeks
 - 2 week interpolation to smooth transitions in rapidly changing trajectories



COVID-19 in Virginia:

Dashboard Updated: 1/26/2021 Data entered by 5:00 PM the prior day

Cases, Hospitalizations and Deaths					
Total Cases* 483,326 (New Cases: 4,707)^		Total Hospitalizations** 20,860		Total Deaths 6,174	

^{*} Includes both people with a positive test (Confirmed), and symptomatic with a known exposure to COVID-19 (Probable) ** Hospitalization of a case is captured at the time VDH performs case investigation. This underrepresents the total number of hospitalizations in

VDH adopted the updated CDC COVID-19 confirmed and probable surveillance case definitions on August 27, 2020. Found

Outbreaks		
Total Outbreaks*	Outbreak Associated Cases	
2,249	55,578	

^{*} At least two (2) lab confirmed cases are required to classify an outbreak

Testing (PCR Only)				
Testing Encounters PCR Only*	Current 7-Day Positivity Rate PCR Only**			
5,079,311	12.5%			

^{*} PCR" refers to "Reverse transcriptase polymerase chain reaction laboratory testing.

^{**} Lab reports may not have been received yet. Percent positivity is not calculated for days with incomplete data

Multisyste Syndron	m Inflammatory ne in Children
Total Cases*	Total Deaths
14	0

^{*}Cases defined by CDC HAN case definition: https://emergency.cdc.gov/han/2020/han00432.asp

Accessed 9:00am January 27, 2021

https://www.vdh.virginia.gov/coronavirus/

New cases represent the number of confirmed and probable cases reported to VDH in the past 24 hours.

Scenarios – Seasonal Effects

- Variety of factors continue to drive transmission rates
 - Seasonal impact of weather patterns, travel and gatherings related to holidays, fatigue with infection control practices
- Plausible levels of transmission can be bounded by past experience
 - Assess transmission levels at the county level since May 2020
 - Use the highest and lowest levels experienced (excluding outliers) as plausible bounds for levels of control achievable
 - Transition from current levels of projection to the new levels over 2 months
- New planning Scenarios:
 - Best of the Past: Lowest level of transmission (10th percentile)
 - Fatigued Control: Highest level of transmission (95th percentile) increased by additional 5%



Scenarios – Novel Variants

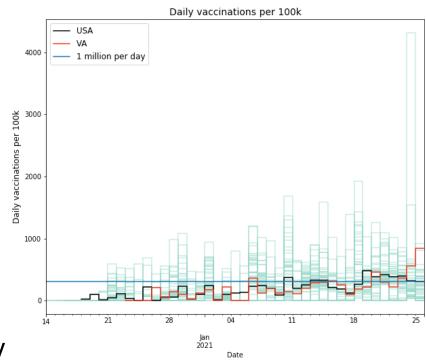
- Several novel variants of SARS-CoV2 are being tracked
 - Some are more transmissible, some may escape immunity from previous natural infection and/or vaccination, others may be more severe
- New Variant B.1.1.7 is best understood and is in Virginia
 - <u>Several different studies</u> have estimated the increase in transmission to be 30-55%, we use 50% increase from the current baseline projection
 - Gradually replace the current transmissibility with the augmented transmissibility over the course of 2 months as estimated by a recent <u>MMWR</u> <u>report from CDC</u>
- Additional planning Scenarios:
 - **NewVariants**: Current projected transmissibility increases gradually over 4 months to level 50% more transmissible



Scenarios – Vaccines

- Vaccination has started, and efforts are underway to increase its pace
 - Exact achievable rollouts and level of coverage are unknown
- Vaccine efficacy varies over course of vaccine
 - FDA EUAs show 50% efficacy achieved 2 weeks after 1st dose, and 95% 2 weeks after 2nd
 - Assuming 3.5 week (average of Pfizer and Moderna) gap between doses
- Vaccine hesitancy poses a future problem
 - Currently demand far outpaces supply so we assume all courses will be administered until we reach the hesitancy threshold, for 50% with 25M per month this is reached in Aug 2021.

US Vaccination Rates



Line represents 1M doses a day goal

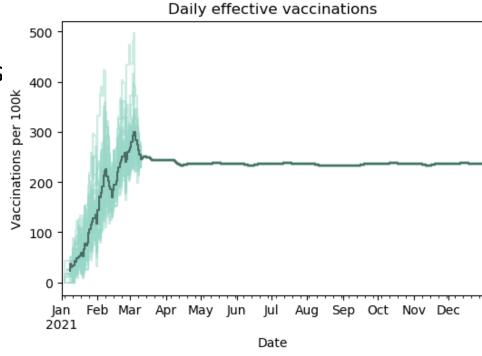
Current rollouts and scenarios inspired by MIDAS Network COVID-19 Scenario Hub: https://github.com/midas-network/covid19-scenario-modeling-hub



Scenarios – Vaccines

- Administration schedule uses actual administration and expected for the future
 - Use history of state-specific doses administered as captured by <u>Bloomberg</u> (up to Jan 24)
 - Future courses based on current goals and consensus
 - Rate: 25M started per month in US, ~250 /100K a day
 - Location: Per capita distribution across all counties
 - Rates in VA for Jan 17-24 are ~420 doses administered /100K a day (some are 2nd doses)

Modeled Vaccine Induced Immunity



Current rollouts and scenarios inspired by MIDAS Network COVID-19 Scenario Hub: https://github.com/midas-network/covid19-scenario-modeling-hub



Scenarios – Seasonal Effects and Vaccines

Three scenarios combine these seasonal effects and use the updated vaccine schedule

- Adaptive: No seasonal effects from base projection
 - If things continue as they are
- Adaptive-FatigueControl: Fatigued control seasonal effects
 - If we revert to slightly worst transmission experienced in last 6 months
- Adaptive-BestPastControl: Best of the past control seasonal effects
 - If we revert to best control experienced in last 6 months
- Adaptive-NewVariants: Boosting of transmissibility from the emergence and eventual ubiquity of more transmissible variants
 - If new variants begin to predominate and boost transmission, this assumes current seasonal affects remain the same (eg like Adaptive)
- Counterfactuals with no vaccine ("NoVax") are provided for comparison purposes

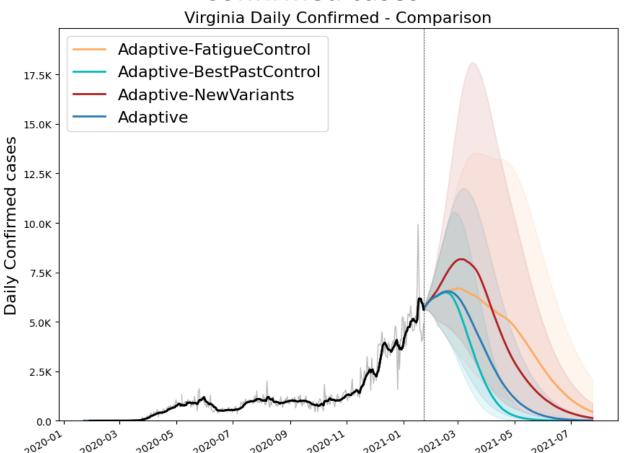


Model Results

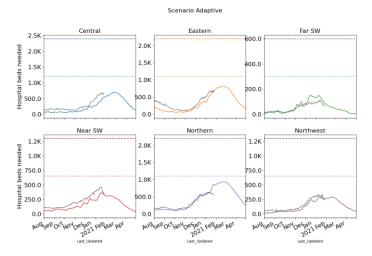


Outcome Projections

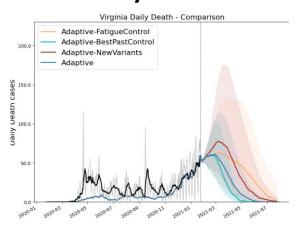
Confirmed cases



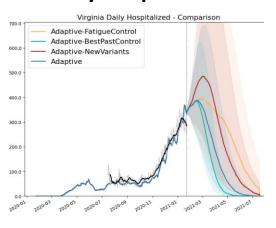
Estimated Hospital Occupancy



Daily Deaths



Daily Hospitalized

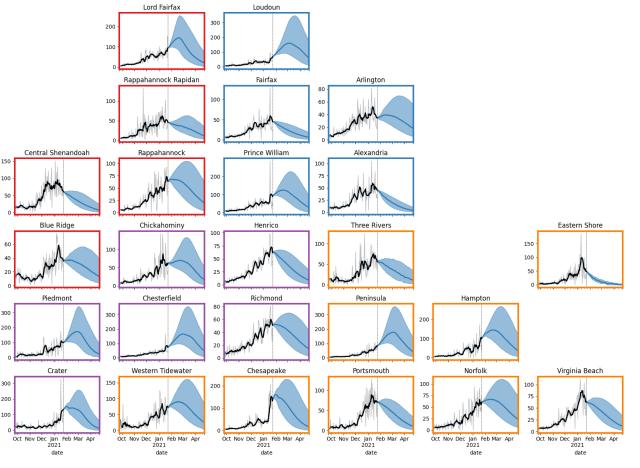




District Level Projections: Adaptive

Adaptive projections by District

- Projections that best fit recent trends
- Daily confirmed cases rate (per 100K) by Region (grey with 7-day average in black) with simulation colored by scenario

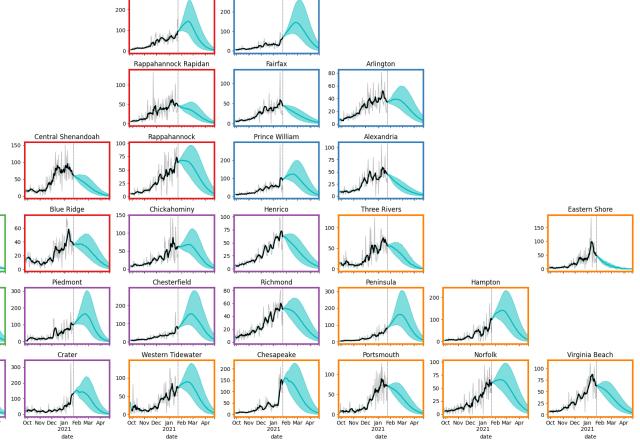




District Level Projections: Adaptive-BestPastControl

Adaptive projections by District

- Projections that best fit recent trends
- Daily confirmed cases rate (per 100K) by Region (grey with 7-day average in black) with simulation colored by scenario

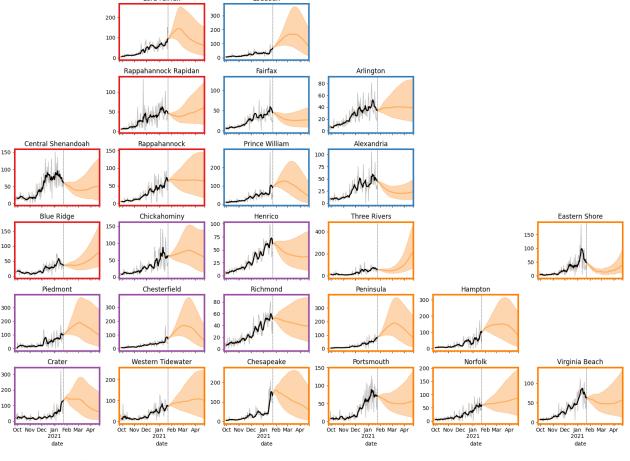




District Level Projections: Adaptive-FatigueControl

Adaptive projections by District

- Projections that best fit recent trends
- Daily confirmed cases rate (per 100K) by Region (grey with 7-day average in black) with simulation colored by scenario



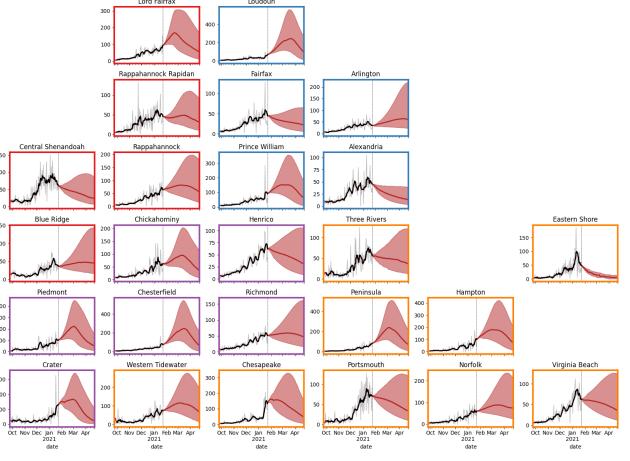


District Level Projections: Adaptive-New Variants

Adaptive projections by District

Projections that best fit recent trends

 Daily confirmed cases rate (per 100K) by Region (grey with 7-day average in black) with simulation colored by scenario

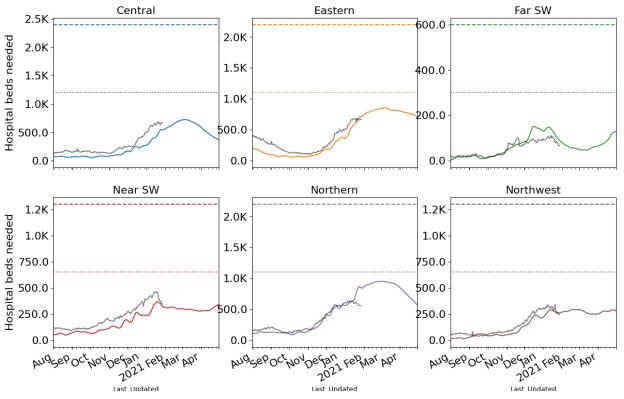




Hospital Demand and Bed Capacity by Region

Capacities* by Region – Adaptive-FatigueControl

COVID-19 capacity ranges from 80% (dots) to 120% (dash) of total beds



Week Ending	Adaptive	Adaptive- Best Past	Adaptive- Fatigued	Adaptive- New
		Control	Control	Variants
1/24/21	41,663	41,660	41,659	41,660
1/31/21	41,820	41,822	41,837	41,972
2/7/21	43,748	43,670	43,766	44,999
2/14/21	45,117	44,903	45,134	48,730
2/21/21	45,721	45,170	45,974	52,764
2/28/21	44,900	42,669	46,529	55,822
3/7/21	42,419	37,356	46,612	57,075
3/14/21	38,396	30,630	45,550	56,326
3/21/21	33,581	23,793	44,381	54,367
3/28/21	28,716	17,572	42,901	50,487
4/4/21	23,803	12,297	41,007	44,623
4/11/21	19,175	8,211	39,219	38,225

If Adaptive-FatigueControl scenario persists:

- Some regions approach initial bed capacity this winter
- Surge bed capacity is unlikely to be reached in coming 4 months

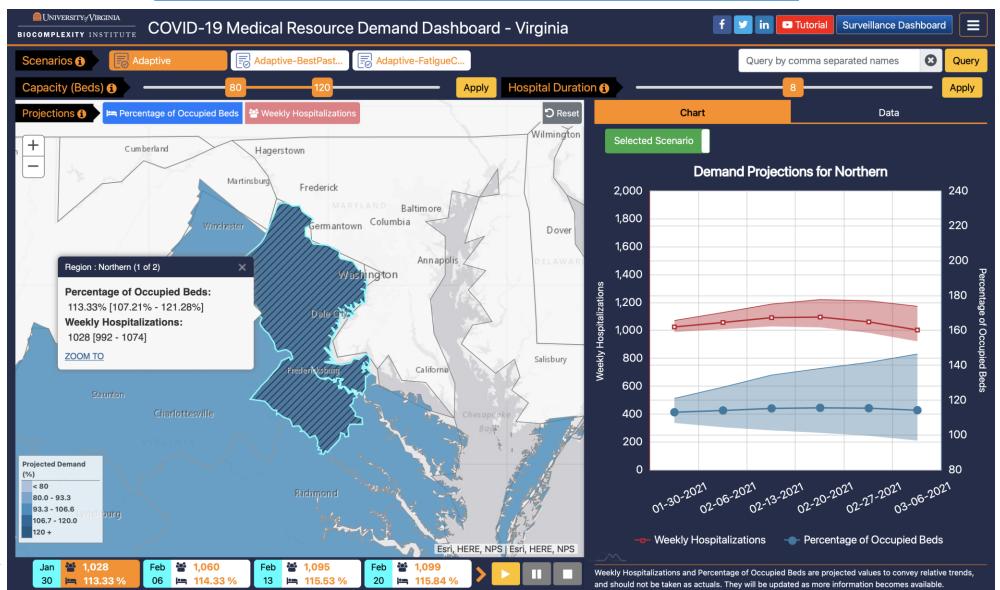
Weekly confirmed cases



^{*} Assumes average length of stay of 8 days 28-Jan-21

Medical Resource Demand Dashboard

https://nssac.bii.virginia.edu/covid-19/vmrddash/



Key Takeaways

Projecting future cases precisely is impossible and unnecessary. Even without perfect projections, we can confidently draw conclusions:

- Case rate growth in Virginia has slowed but remains high
- VA mean weekly incidence down sharply 54/100K from 72/100K, as national levels continued to decline (to 45/100K from 54/100K)
- Projections are mixed across commonwealth with some short-term growth at state level mainly driven by central section of the state
- Recent updates:
 - Adjusted projection window to account for shifting trends
 - Scenarios based on past control levels (best and fatigued) and emerging new variants with enhanced transmissibility
 - Further updates to vaccination schedules, accounts for partial protection from first dose and merges observed doses with goals for future vaccine administration
- The situation is changing rapidly. Models will be updated regularly.



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NSSAC. PatchSim: Code for simulating the metapopulation SEIR model. https://github.com/NSSAC/PatchSim (Accessed on 04/10/2020).

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Biocomplexity Institute. COVID-19 Surveillance Dashboard. https://nssac.bii.virginia.edu/covid-19/dashboard/

Google. COVID-19 community mobility reports. https://www.google.com/covid19/mobility/

Biocomplexity page for data and other resources related to COVID-19: https://covid19.biocomplexity.virginia.edu/



Questions?

Points of Contact

Bryan Lewis brylew@virginia.edu

Srini Venkatramanan srini@virginia.edu

Madhav Marathe marathe@virginia.edu

Chris Barrett@virginia.edu

Biocomplexity COVID-19 Response Team

Aniruddha Adiga, Abhijin Adiga, Hannah Baek, Chris Barrett, Golda Barrow, Richard Beckman, Parantapa Bhattacharya, Andrei Bura, Jiangzhuo Chen, Patrick Corbett, Clark Cucinell, Allan Dickerman, Stephen Eubank, Arindam Fadikar, Joshua Goldstein, Stefan Hoops, Ben Hurt, Sallie Keller, Ron Kenyon, Brian Klahn, Gizem Korkmaz, Vicki Lancaster, Bryan Lewis, Dustin Machi, Chunhong Mao, Achla Marathe, Madhav Marathe, Fanchao Meng, Henning Mortveit, Mark Orr, Joseph Outten, Akhil Peddireddy, Przemyslaw Porebski, SS Ravi, Erin Raymond, Jose Bayoan Santiago Calderon, James Schlitt, Aaron Schroeder, Stephanie Shipp, Samarth Swarup, Alex Telionis, Srinivasan Venkatramanan, Anil Vullikanti, James Walke, Amanda Wilson, Dawen Xie



Supplemental Slides



Estimating Daily Reproductive Number

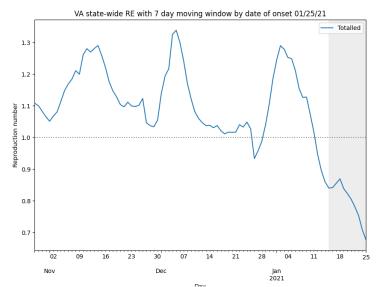
Jan 16th Estimates

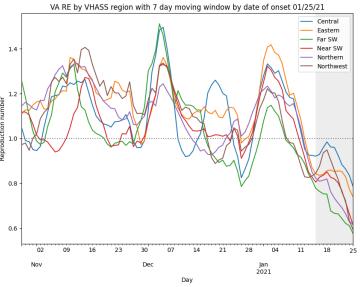
Region	Date of Onset R _e	Date Onset Diff Last Week
State-wide	0.842	-0.216
Central	0.929	-0.182
Eastern	0.835	-0.235
Far SW	0.763	-0.167
Near SW	0.827	-0.210
Northern	0.809	-0.300
Northwest	0.876	-0.053

Methodology

- Wallinga-Teunis method (EpiEstim¹) for cases by date of onset
- Serial interval: 6 days (2 day std dev)
- Recent estimates may be unstable due to backfill

1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

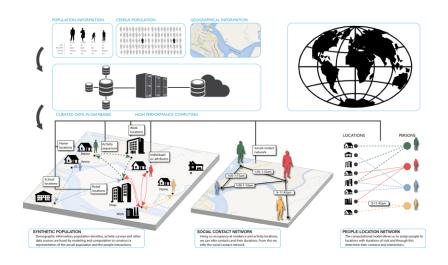




Agent-based Model (ABM)

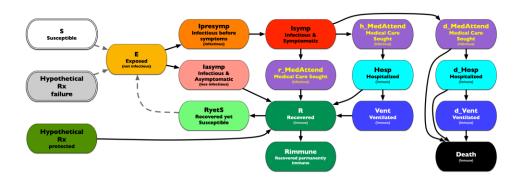
EpiHiper: Distributed network-based stochastic disease transmission simulations

- Assess the impact on transmission under different conditions
- Assess the impacts of contact tracing



Synthetic Population

- Census derived age and household structure
- Time-Use survey driven activities at appropriate locations



Detailed Disease Course of COVID-19

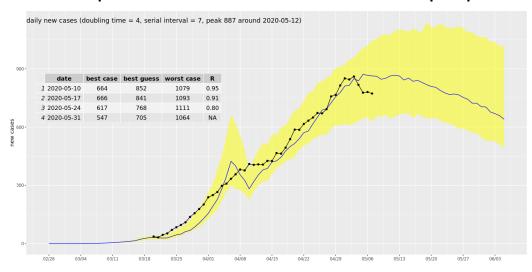
- Literature based probabilities of outcomes with appropriate delays
- Varying levels of infectiousness
- Hypothetical treatments for future developments



ABM Social Distancing Rebound Study Design

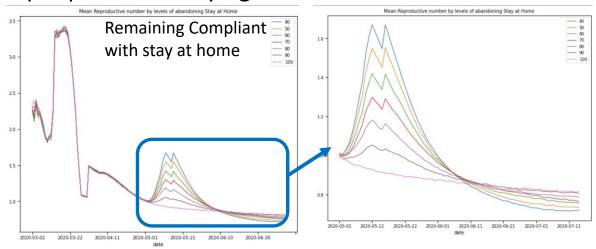
Study of "Stay Home" policy adherence

- Calibration to current state in epidemic
- Implement "release" of different proportions of people from "staying at home"



Calibration to Current State

- Adjust transmission and adherence to current policies to current observations
- For Virginia, with same seeding approach as PatchSim



Impacts on Reproductive number with release

- After release, spike in transmission driven by additional interactions at work, retail, and other
- At 25% release (70-80% remain compliant)
- Translates to 15% increase in transmission, which represents a 1/6th return to pre-pandemic levels

